

Banfoxanthone, a new prenylated xanthone from the stem bark of *Garcinia ovalifolia* (Guttiferaceae)

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ABSTRACT

A detailed chemical investigation of the secondary metabolites from the extract of the stem bark of *Garcinia ovalifolia* led to the isolation of one new prenylated xanthone named banfoxanthone and five known compounds, namely friedeline, canophyllal, ovalifoloneA, 3-methoxycheffouxanthone, endodesmiadol. Prenyated xanthones isolated from *Garcinia ovalifolia* and others species of genus *Garcinia* appear to be useful as chemotaxonomic markers in *Garcinia*.

INTRODUCTION

The genus *Garcinia* (Guttiferae) is known to produce a variety of biologically active metabolites such as polyisoprenylated benzophenones (Meli Lannang et al., 2010; Gustafson et al., 1992), xanthones (Louh et al., 2008) as well as triterpenoids (Nguyen et al., 2011; Meli Lannang et al., 2008). Some of them exhibited a wide range of biological activities such as cytotoxic, anti-inflammatory, anti-diabetes, anti-fungal, anti-microbial, anti-oxidant and anti HIV activities (Hiroyuki et al., 1996; Nkengfack et al., 2002; Hay et al., 2004; Merza et al., 2004; Lannang et al., 2005). In the continuation of our search for bioactive substances from *Garcinia* species, we have investigated the hexane and methanol extracts of the stem bark of *Garcinia ovalifolia*. *G. ovalifolia* is a tree up to 10–15 m on high, with yellow sticky latex, generally distributed in fringing forests and river banks in West and central Africa (Gustafson et al., 1992), Asia, New Caledonia and Polynesia (Ampofo and Waterman, 1986).

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We describe herein the isolation and structure elucidation of minor constituents from *G. ovalifolia*, which included a new prenylated xanthone namely banfoxanthone (**1**). Together with three known pentacyclic triterpenes (**2,4,6**), one known benzophenone (**3**) and one known xanthone (**5**).

Experimental

General experimental procedures

Optical rotations were measured in methanol solution on a JASCO digital polarimeter (model DIP-3600). The specific rotation is given in deg cm² g⁻¹. IR spectra were recorded in CHCl₃ on a JASCO A-302 IR spectrophotometer. The ¹H, ¹³C, and 2D-NMR spectra were recorded on a Bruker AMX-500 spectrometer using acetone-d₆ as solvent. Homonuclear 1H–1H connectivity were determined by using the COSY 458 experiment. One-bond 1H–¹³C connectivity were determined by HMQC. Two and three-bond 1H–¹³C connectivity are determined by HMBC experiment. Proton and ¹³C chemical shifts are reported in δ (ppm). Coupling constants (J) were measured in Hz. The EIMS were recorded on a double-focusing mass spectrometer (Varian MAT 311A). HREIMS were recorded on a JEOL HX 110 mass spectrometer.

Column chromatography was carried out with silica gel 60 (70–230 and 240–300 mesh sizes, E. Merck) Precoated silica gel TLC plates (E. Merck, F254) were used to check the purity of compounds, and ceric sulfate spray reagent was used for the visualization of compounds on TLC plates.

Plant material

The stem bark of *G. ovalifolia* was collected from the village Banganfokam, in the west region of Cameroon in February 2010, and identified by the botanist Dr. Tchiengue Barthelemy. A voucher specimen was deposited at the National Herbarium in Yaounde, Cameroon under Ref. N° 55523/HNC/CAM/Nkambé.

Extraction and isolation of natural products

The air-dried and powdered stem bark of *G. ovalifolia* (1.7kg) was separately extracted at room temperature for 72H successively with hexane and methanol. The concentrations of the solutions under reduced pressure yielded 37g of hexane extract and 344g of methanol extract.

A part of the MeOH extract (300g) was suspended in 2000ml of aqueous MeOH (MeOH/H₂O, 9:1) and extracted with n-hexane (3 x 500ml). The aqueous layer was then diluted with 60 % MeOH and extracted with CH₂Cl₂ (3 x 500ml), then with EtOAc. The n-hexane and CH₂Cl₂ extracts were combined on the basis of TLC profile. This combined fraction was purified by column chromatography over silica gel 60 (230-400mesh) and preparative TLC using a gradient system of n-hexane, CH₂Cl₂, ethyl acetate and MeOH, yielding friedeline (**2**) (15.5mg), canophyllal (**3**) (8.5mg), ovalifolone A (**4**) (12.0mg), 3-methoxycheffouxanthone (**5**) (12.0mg).

The n-hexane extract (35g) was chromatographed over a column (5 x 80cm) of silica gel 60 (230-400mesh) eluting with a mixture of n-hexane/EtOAc in increasing polarity (10:0, 1L; 8:2, 1L; 6:4, 1L; 4:6, 750 mL; 0:10 500 mL). A total of 130 fractions were collected and subsequently combined into four series of fractions A-D using their TLC profile. Further column chromatography of series A eluted with hex/EtOAc (9.5:0.5 and 9:1) yielded endodesmiadol (**6**) (11mg). The series B was subjected to silica gel column chromatography and eluted with gradient of hex/EtOAc (9.5:0.5 and 9:1) to obtain endodesmiadol (**6**) (30mg) and banfoxanthone (**1**) (10mg).

RESULTS AND DISCUSSION

Identification of natural products

As a continuation of our previous phytochemical investigation of the stem bark of *Garcinia ovalifolia*, the present study report the characterization of a new prenylated xanthone namely banfoxanthone (**1**).

Banfoxanthone (**1**) was isolated as yellow needle crystals. The ESI mass spectrum in MeOH/H₂O showed the M-1 ion at *m/z* 311.0926 and the 2M-1 ion at *m/z* 623.1924 suggesting the molecular formula to be C₁₈H₁₆O₅. The UV spectrum of banfoxanthone (**1**) showed absorption bands at λ_{\max} 238.00;

248.92; 264.90 and 313.85 nm confirming a xanthone derivative (Nkengfack *et al.*, 2002). The IR spectrum exhibited absorption bands at 3430, 2925, 1721 and 1630 cm⁻¹ suggesting the xanthone skeleton with a chelated carbonyl (Federicio *et al.*, 2001).

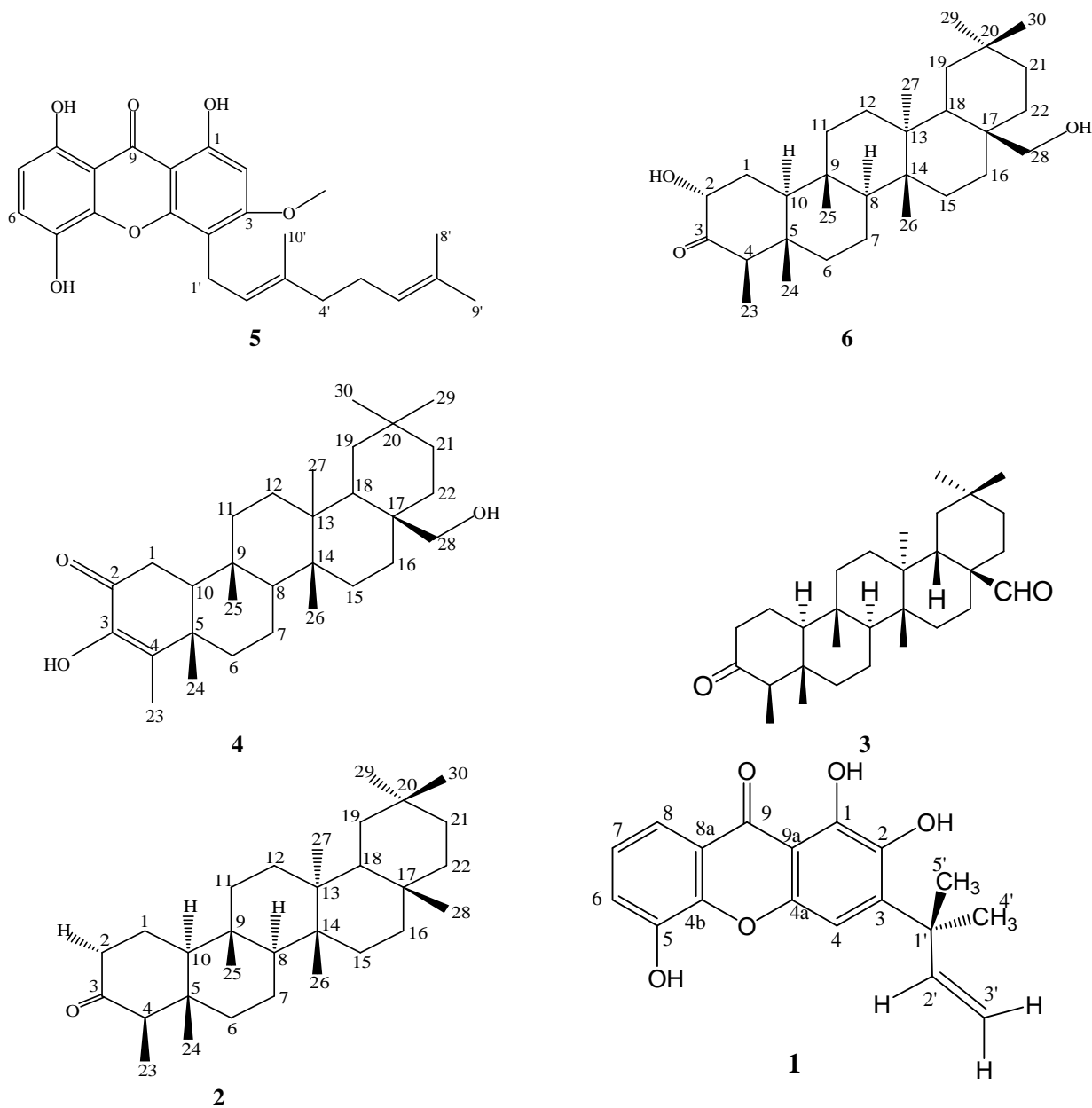
The ¹H and ¹³CNMR spectra of compound (**1**) (Table 1) showed a singlet at δ_H 12.89 assigned to an hydroxyl group (OH-1) which chelated to a carbonyl resonating at δ_C 184.0 (C-9). They also showed an aromatic proton singlet at δ_H 7.33 which was assigned to the C-4 position on the basis of the HMBC correlation (Fig. 2) between H-4 and δ_C 147.0 (C-4a). An ABC type aromatic proton system was observed at δ_H 7.72 (1H, dd, H-8), 7.37 (1H, dd, H-6) and 7.30 (1H, t, H-7) suggesting the presence of three adjacent protons in the same ring. The HMBC spectrum showed correlations between proton at δ_H 7.30 (H-7) and carbons at δ_C 116.5 (C-8) and 137.9 (C-8a), proton at δ_H 7.37 (H-6) and carbons at δ_C 148.0 (C-5) and 142.0 (C-4b). The ¹H and ¹³CNMR spectra also showed signals at δ_H 6.33 (1H, dd, H-2'), 5.00 (2H, d, H-3') and 1.5 (6H, s, CH₃-4' and CH₃-5') suggesting the presence of a prenyl moiety which was connected to the xanthone skeleton using not the usual tail position, but instead an unusual head position (1, 1-dimethylallyl). On the basis of the HMBC spectrum, correlations observed (Fig. 2) between the two methyl protons CH₃-4' and CH₃-5' (δ_H 1.5) and carbon signals at δ_C 130.0 (C-3), 123.0 (C-4) and 41.0 (C-1'), and between the singlet signal at δ_H 7.33 (H-4) and carbon signals at δ_C 41.0 (C-1'), 146.0 (C-2) and 147.0 (C-4a) allowed to link the unusual prenyl (1, 1-dimethylallyl group) at the C-3 position of the xanthone skeleton. More correlations observed between δ_H 12.89 (OH-1) and carbon signals at δ_C 154.0 (C-1), δ_C 109.0 (C-9a) and 130.0 (C-3), further supported the substitution pattern in ring B. From the above interpretation of spectral data, this compound was established to be a new xanthone derivative, 1, 2, 5-trihydroxy-3-(1', 1'-dimethylallyl) xanthone, named as banfoxanthone(**1**).

Previous work

Previous phytochemical investigations on *G. ovalifolia* have resulted in the isolation of a variety of secondary metabolites which mainly included Guttiferone E (Gustafon *et al.*, 1992), ovalifolone (A), ovalifolone (B), (Lannang *et al.*, 2013), endodesmiadol and friedeline (Ngouamegne *et al.*, 2008), isoxanthochimol (Louh *et al.*, 2008), 3-methoxycheffouxanthone (Meli *et al.*, 2010), canophyllol (Ngouamegne *et al.*, 2008), canophyllal (Ngouamegne *et al.*, 2008), gallic acid (Sudjaroen *et al.*, 2012), garcinane (Lannang *et al.*, 2013).

Chemotaxonomic significance

Previous work on this species have permitted to isolate endodesmiadol, friedeline, canophyllol, canophyllal and the same natural products have been isolated in the species belonging to the Guttiferae family. The same natural product, isoxanthochimol has been isolated also in the species *Garciniapolyantha* (Louh *et al.*, 2008). Prenylatedxanthenes appear to be useful as chemotaxonomic markers in *Garcinia*.



Structures of compounds 2-6
Fig.1: Structure of compound (1).

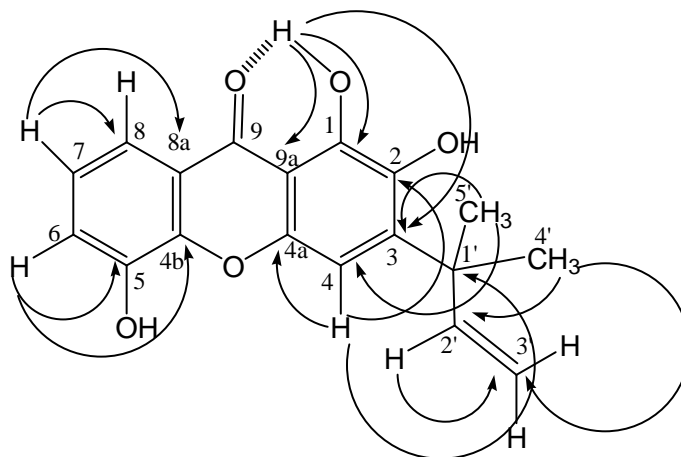


Fig. 2: Key HMBC correlations of compound (1).

Table 1: The ¹H NMR and ¹³C NMR spectral data and HMBC correlations of compound 1 (acetone-d₆, 500 MHz for ¹H and 125 MHz for ¹³C).

Position	¹ H NMR	¹³ C NMR	HMBC (H-C)
1	12.89 (OH, s)	154.0	C-1, C-9a, C-3
2	9.00 (OH, s)	146.0	
3	-	130.0	
4	7.33 (1H, s)	123.0	C-4a, C-1', C-2
4a	-	147.0	
4b	-	142.0	
5	9.00 (OH, s)	148.0	
6	7.37 (1H, dd, J = 7.9; 1.6 Hz)	125.0	C-5, C-4a
7	7.30 (1H, t, J = 7.9 Hz)	122.0	C-8, C-8a
8	7.72 (1H, dd, J = 7.9; 1.6 Hz)	116.0	
8a	-	137.9	
9	-	184.0	
9a	-	109.0	
1'	-	41.0	
2'	6.33 (1H, dd)	148.0	C-3'
3'	5.00 (2H, d)	111.0	
4'	1.50 (3H, s)	26.5	C-1', C-3, C-4, C-2', C-3'
5'	1.50 (3H, s)	26.5	C-1', C-3, C-4, C-2', C-3'

CONCLUSION

From the stem bark of *Garcinia ovalifolia*, a new prenylated xanthone namely banfoxanthone (**1**) together with three known pentacyclic triterpenes (friedelan(**2**), ovalifoloneA(**4**), endodesmiadol(**6**)), one known benzophenone (canophyllal(**3**)) and one known xanthone (3-methoxycheffouxanthone(**5**)) have been isolated. According to the previous works done on some species of genus *Garcinia* and others species belonging to the guttiferace family, we finally conclude that prenylated xanthones appear to be useful as chemotaxonomic markers in *Garcinia*.

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Author(s)' Statement(s)

Competing Interests

The author(s) declare(s) no conflict of interest and competing interests in this work.

Informed Consent, Ethical Approvals

Plant material used in this work is commercially available and does not need any informed consent from the local populations.

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